Draft Assessment Report

Evaluation of Active Substances

Plant Protection Products

Prepared according to **Retained Regulation (EC) 1107/2009**
as it applies in Great Britain

Metalaxyl-M

Volume 1

GB Article 7 Amendment of Approval

Great Britain

Janurary 2024

Version History

When	What
January 2024	Initial DAR

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Level 1

Metalaxyl-M

1. STATEMENT OF SUBJECT MATTER AND PURPOSE FOR WHICH THIS REPORT HAS BEEN PREPARED AND BACKGROUND INFORMATION ON THE APPLICATION

1.1. CONTEXT IN WHICH THIS DRAFT ASSESSMENT REPORT WAS PREPARED

1.1.1. Purpose for which the draft assessment report was prepared

This draft assessment report (DAR) has been prepared to evaluate the application submitted to amend the approval of the pesticidal active substance metalaxyl-M under Article 7 of retained Regulation (EC) No. 1107/2009 in Great Britain (GB). The application was submitted by Syngenta, the producer of the active substance hereafter referred to as the "applicant".

The approval of metalaxyl-M was renewed in the European Union (EU) in June 2020. The UK was an EU Member State (MS) at that time and therefore the renewal of approval of metalaxyl-M applied directly in the UK. Metalaxyl-M was renewed under Commission Implementing Regulation (EU) 2020/617 which specified the following restriction according to the provisions in Article 6 (1) of Regulation (EC) No 1107/2009:

When used for seed treatment, only the treatment of seeds intended to be sown in greenhouses may be authorised.

The application for amendment has been submitted to remove the restriction on the approval of metalaxyl-M. The applicant has submitted the relevant data and information within the application.

In addition, the applicant has submitted new toxicology data to support a change to the maximum level of the impurity CGA226048. This impurity is of toxicological concern and the approval currently lists a maximum content of 0.18 g/kg. The applicant has submitted information to increase this level to 15 g/kg, as originally proposed at EU renewal.

The applicant has also submitted data to remove metabolite NOA409045 as a relevant groundwater metabolite. In addition, the applicant proposes to amend the EFSA conclusion regarding relevance of the groundwater metabolite CGA108906.

For ecotoxicology, a revised birds and mammals risk assessment has been submitted including proposal to review the bird reproductive endpoint (NOEL) concluded by EFSA in 2015.

For the application, the applicant has considered two representative formulations, WAKIL XL (A9873C) and VIBRANCE SB (A20607B). These formulated products were not the representative formulations considered for the renewal of approval but are relevant for use of metalaxyl-M in GB.

WAKIL XL and VIBRANCE SB are both mixed active products. HSE has considered only information and data for metalaxyl-M in the DAR. For future authorisation of these products in GB, a full assessment would be required.

The applicant has presented the information and data for the representative formulations within a draft registration report (dRR) rather than a dossier in the format agreed by the Organisation for Economic Co-operation and Development (OECD). HSE has accepted the submission. HSE has presented the risk assessment for the representative formulations within the applicant's dRR, see the individual documents for further information.

Note that as of 1st January 2024, The Retained EU Law (Revocation and Reform) Act 2023 has taken effect and retained EU law are now known as assimilated law. As this assessment has been prepared prior to the Retained EU Law Act taking effect, assessment may still refer to "retained" regulation as opposed to "assimilated".

1.1.2. Regulatory history for use in Plant Protection Products

Metalaxyl-M is an approved active substance that was included in Annex I to Council Directive 91/414/EEC concerning the placing of plant protection products on the market, by Commission Directive 2002/64/EC6. Metalaxyl-M was, therefore, deemed to be approved under Regulation (EC) No 1107/2009 and was listed in Part A of the Annex to Commission Implementing Regulation (EU) No 540/20117.

The approval of Metalaxyl-M was renewed on 01 June 2020 under Commission Implementing Regulation (EU) 2020/617.

For the renewal of the approval of metalaxyl-M, the rapporteur Member State (RMS) was Belgium and the co-rapporteur Member State (co-RMS) was Greece. The RMS finalised its examination, in the form of a renewal assessment report (RAR) in November 2013. This Report was sent to the Commission and the European Food Safety Authority (EFSA) on 13 November 2013 and included a recommendation concerning the decision to be taken with regard to the renewal of the approval of metalaxyl-M for the supported uses.

In accordance with Article 16 of Commission Regulation (EU) No 1141/2010, the Commission requested the EFSA to arrange an expert consultation on the rapporteur Member State's renewal assessment report and to deliver its conclusions. EFSA also launched a public consultation on the RAR. The 2014 RAR can be viewed on the openEFSA Questions page on the EFSA website (Output Number: ON-3999, Question Number: EFSA-Q-2020-00666). The 2015 EFSA conclusion can be viewed under EFSA publications (Question number: EFSA-Q-2020-00666).

According to the provisions of Article 17 of Regulation (EU) No 1141/2010, the Commission referred a draft review report on the renewal of approval to the Standing Committee on Plants, Animals, Food and Feed, for examination on 14 July 2015. The draft review report on renewal of approval was finalised by the Standing Committee on 24 March 2020. The renewal report contains the conclusions of the final examination by the Standing Committee which support the Commission Implemeneting Regulation for the renewal of approval.

1.1.3. Evaluations carried out under other regulatory contexts

None.

1.2. APPLICANT INFORMATION

1.2.1. Name and address of applicant(s) for approval of the active substance

Address : Syngenta UK Limited
CPC4, Capital Park
Fulbourn
Cambridge
CB21 5XE
United Kingdom

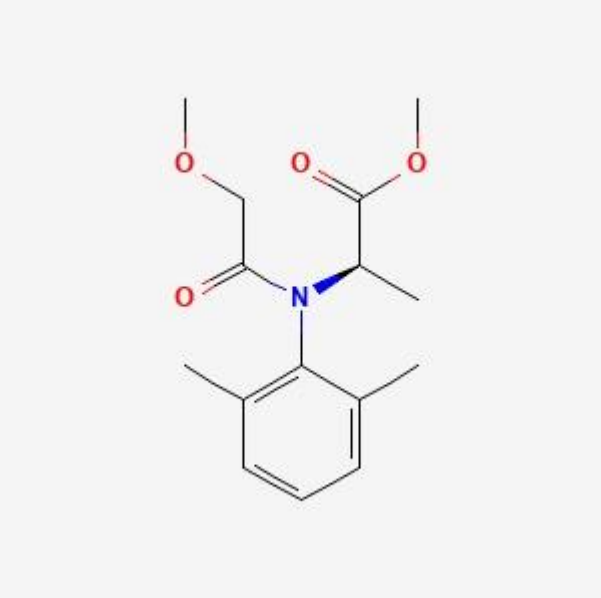
Contact person : Mr [redacted]
Head of Regulatory UK & Ireland
Syngenta UK Limited
CPC4, Capital Park
Fulbourn
Cambridge
CB21 5XE
Tel: [redacted]
E-mail: [redacted]

1.2.2. Producer or producers of the active substance

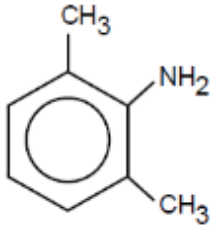
Not relevant. Syngenta are the sole notifier for the active substance.

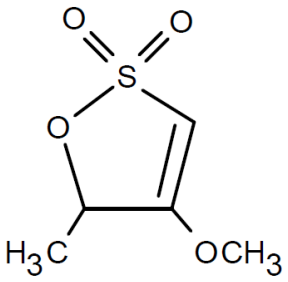
1.3. IDENTITY OF THE ACTIVE SUBSTANCE

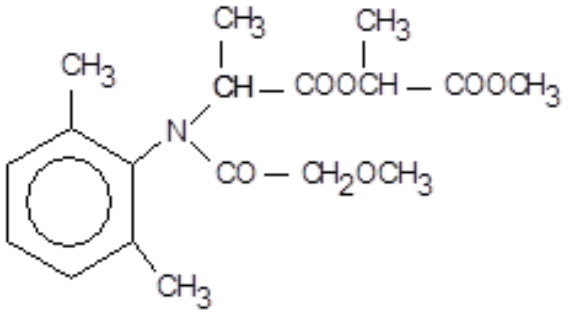
1.3.1. Common name proposed or ISO-accepted and synonyms	Metalaxyl-M
1.3.2. Chemical name (IUPAC and CA nomenclature)	
IUPAC	methyl N-(methoxyacetyl)-N-(2,6-xylyl)-D-alaninate
CA	methyl (R)-N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alaninate
1.3.3. Producer's development code number	CGA329351
1.3.4. CAS, EEC and CIPAC numbers	
CAS	70630-17-0
EEC	615-135-6
CIPAC	580

1.3.5. Molecular and structural formula, molecular mass	
Molecular formula	$C_{15}H_{21}NO_4$
Structural formula	
Molecular mass	279.33 g/mol

1.3.6. Method of manufacture (synthesis pathway) of the active substance	Confidential Information. See Volume 4.
1.3.7. Specification of purity of the active substance in g/kg	Min. 920 g/kg metalaxyl-M (CGA329351, R-isomer)), methyl R-2-{[(2,6-dimethylphenyl)methoxyacetyl]amino}propionate.
1.3.8. Identity and content of additives (such as stabilisers) and impurities	
Additives	Confidential Information. See Volume 4.
Significant impurities	Confidential Information. See Volume 4.

Relevant impurities	Technical metalaxyl-M contains the following relevant impurities : 2,6-dimethyl-phenylamine (2,6-DMA; impurity CGA 72649) at a maximum level of 0.5 g/kg IUPAC nomenclature : 2,6-dimethyl-phenylamine CA nomenclature : 2,6-dimethylbenzenamine ISO common name : - CAS No : 87-62-7 EEC No : 201-758-7 (EINECS) CIPAC No : - Molecular formula : C8H11N Molecular mass : 121.2 g/mol Sutructural Formula:  Specification : ≤ 0.5 g/kg 4-methoxy-5-methyl-5H-[1,2]oxathiole 2,2-dioxide (impurity CGA363736) at a maximum level of 1 g/kg IUPAC nomenclature : 4-methoxy-5-methyl-5H-[1,2]oxathiole 2,2-dioxide CA nomenclature : 4-methoxy-5-methyl-5H-[1,2]oxathiole 2,2-dioxide ISO common name : - CAS No : not available EEC No : not available

	CIPAC No : - Molecular formula : $C_5H_8O_4S$ Molecular mass : 164.2 g/mol Structural formula :  Specification : ≤ 1 g/kg **NOTE the following impurity was considered relevant however, as a result of this assessment, is no longer considered relevant.** 2-[(2,6-dimethyl-phenyl)-(2- methoxyacetyl)-amino]-propionic acid 1-methoxycarbonyl- ethyl ester (impurity CGA 226048) at a maximum level of 0.18 g/kg IUPAC nomenclature: 2-[(2,6-dimethyl-phenyl)-(2- methoxyacetyl)-amino]-propionic acid 1-methoxycarbonyl- ethyl ester CA nomenclature: - ISO common name: - CAS Number: n/a EEC Number: n/a CIPAC No: n/a Molecular Formula:$C_{18}H_{25}O_6N$ Molecular Mass: 351.4 g/mol

	Structural Formula:  Specification: ≤ 0.18 g/kg
1.3.9. Analytical profile of batches	Confidential information, see Volume 4.

1.4. INFORMATION ON THE PLANT PROTECTION PRODUCT

	Formulation 1 'Wakil XL'	Formulation 2 'Vibrance SB'
1.4.1. Applicant	Syngenta	Syngenta
1.4.2. Producer of the plant protection product	Confidential data, see Volume 4	Confidental data, see Volume 4
1.4.3. Trade name or proposed trade name and producer's development code number of the plant protection product	Wakil XL (A9873C)	Vibrance SB (A2060B)
1.4.4. Detailed quantitative and qualitative information on the composition of the plant protection product		
Composition of the plant protection product	Confidential Data see Volume 4	Confidential Data see Volume 4
Information on the active substances	Confidential Data see Volume 4	Confidential Data see Volume 4
Information on safeners, synergists and co-formulants	Confidential Data see Volume 4	Confidential Data see Volume 4
1.4.5. Type and code of the plant protection product	Wettable Granule Code: WG	Flowable Concentrate for Seed Treatment Code: FS
1.4.6. Function	Fungicide	Fungicide
1.4.7. Field of use envisaged	Seed Treatment	Seed Treatment
1.4.8. Effects on harmful organisms	Metalaxyl-M inhibits mycelial growth and spore formation both in vivo and in vitro. Foliar pathogens are inhibited only after they have penetrated the leaves. Metalaxyl-M inhibits the fungi by selectively interfering with the synthesis of ribosomal RNA. Metalaxyl-M itself is the active ingredient. Metalaxyl-M is a systemic fungicide taken up very rapidly following leaf application. Translocation of the compound is primarily acropetal. This acropetal or upward movement is a gradual and continuous process, thus providing additional fungicidal activity and disease control as new plant growth occurs.	

1.5. DETAILED USES OF THE PLANT PROTECTION PRODUCT

1.5.1. Details of representative uses

PPP (product name/code):	WAKIL XL / A9873C	Formulation type:	WG (a, b)
Active substance 1:	Cymoxanil	Conc. of a.s. 1:	100 g/kg (c)
Active substance 2:	Fludioxonil	Conc. of a.s. 2:	50 g/kg (c)
Active substance 3:	Metalaxyl-M	Conc. of a.s. 3:	169.6 g/kg (c)
Applicant:	Syngenta	Professional use:	☒

Member state(s)	Crop and/ or situation	F G or I	Pests or Group of pests controlled	Application				Application rate				PHI (days)	Remarks:
				Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	g product / 100 kgs seeds	g a.s./100kg seeds 1) Metalaxyl-M 2) Cymoxanil 3) Fludioxonil	g a.s./ha 1) Metalaxyl-M 2) Cymoxanil 3) Fludioxonil	Slurry volume mL/100 kg min / max		
GB	Combining peas [PIBSS]	I	*Peronospora viciae, Ascochyta complex : Ascochyta pisi, Mycosphaerella pinodes, Phoma medicaginis var. Pinodella, Pythium spp.*	Seed treatment	BBCH 00	1	n/a	200	1) 33.9 2) 20 3) 10	1) 67.8 2) 40 3) 20 Note: 95 g metalaxyl-M/ha assumed for GB environmental exposure assessment for use on combining and vining peas	3500	n/a	Seeding rate maximum 200 kg seeds/ha TGW: 250 g Use: Field Varieties of common pea (*Pisum sativum*) harvested when fully mature
		F		Sowing	BBCH 00								
		n.a.		Trans-planting	n.a.								
GB	Vining peas [PIBSS]	I	*Peronospora viciae, Ascochyta complex: Ascochyta pisi, Mycosphaerella pinodes, Phoma medicaginis var.*	Seed treatment	BBCH 00	1	n/a	200 g product/ 100 kgs seeds Or	1) 33.9/ 30.15 2) 20/ 17.78 3) 10/ 8.89	1) 76.3/ 67.8 2) 45/ 40 3) 22.5/20	3500	n/a	Seeding rate: maximum 225 kg seeds/ha TGW:min 225 g
		F		Sowing	BBCH 00								

Member state(s)	Crop and/ or situation	F G or I	Pests or Group of pests controlled	Application				Application rate				PHI (days)	Remarks:
				Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	g product / 100 kgs seeds	g a.s./100kg seeds 1) Metalaxyl-M 2) Cymoxanil 3) Fludioxonil	g a.s./ha 1) Metalaxyl-M 2) Cymoxanil 3) Fludioxonil	Slurry volume mL/100 kg min / max		
		n.a.	*pinodella Pythium spp.,*	Trans-planting	n.a.			*40 g product/100 000 seeds*		Note: 95 g metalaxyl-M/ha assumed for GB environmental exposure assessment for use on combining and vining peas			Use: Field Varieties of common pea (*Pisum sativum*) harvested green for canning, freezing or marketing fresh. *Seeding density: 1000000 seeds/ha*

Please note: Blue colour font - *Alternative dose expression*

Remarks table heading:

(a) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(b) Catalogue of pesticide formulation types and international coding system CropLife International Technical Monograph n°2, 6th Edition Revised May 2008
(c) g/kg or g/l
(d) Select relevant
(e) Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1
(f) No authorization possible for uses where the line is highlighted in grey, Use should be crossed out when the notifier no longer supports this use.

Remarks columns:

1 Numeration necessary to allow references
2 Use official codes/nomenclatures of EU Member States
3 For crops, the EU and Codex classifications (both) should be used; when relevant, the use situation should be described (e.g. fumigation of a structure)
4 F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application
5 Scientific names and EPPO-Codes of target pests/diseases/ weeds or, when relevant, the common names of the pest groups (e.g. biting and sucking insects, soil born insects, foliar fungi, weeds) and the developmental stages of the pests and pest groups at the moment of application must be named.
6 Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated.
7 Growth stage at first and last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
8 The maximum number of application possible under practical conditions of use must be provided.
9 Minimum interval (in days) between applications of the same product
10 For specific uses other specifications might be possible, e.g.: g/m³ in case of fumigation of empty rooms. See also EPPO-Guideline PP 1/239 Dose expression for plant protection products.
11 The dimension (g, kg) must be clearly specified. (Maximum) dose of a.s. per treatment (usually g, kg or L product / ha).
12 If water volume range depends on application equipments (e.g. ULVA or LVA) it should be mentioned under “application: method/kind”.
13 PHI - minimum pre-harvest interval
14 Remarks may include: Extent of use/economic importance/restrictions

PPP (product name/code):	VIBRANCE SB / A20607B	Formulation type:	FS [a, b]
Active substance 1:	Fludioxonil	Conc. of a.s. 1:	22.5 g/L [c]
Active substance 2:	Metalaxyl-M	Conc. of a.s. 2:	14.4 g/L [c]
Active substance 3:	Sedaxane	Conc. of a.s. 3:	15 g/L [c]
Applicant:	Syngenta	Professional use:	☒

Member state(s)	Crop and/ or situation	F, Fn, Fpn G, Gn, Gpn or I	Pests or Group of pests controlled	Application				Application rate				PHI (days)	Remarks:
				Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	ml product / seed unit	Max g a.s./100 kg seeds 1) Fludioxonil 2) Metalaxyl-M 3) Sedaxane	Max g a.s./ha 1) Fludioxonil 2) Metalaxyl-M 3) Sedaxane	Max µg a.s./seed 1) Fludioxonil 2) Metalaxyl-M 3) Sedaxane		
GB	Beet (Sugar (BEAVA) and fodder (BEAVC) beet)	I	Damping-off diseases (*Pythium ultimum* [PYTHUL], *Pleospora betae/P betae* [PLEOBJ], *Thanatephorus cucumeris / Rhizoctonia solani* [RHIZSO])	Seed treatment	BBCH 00 Jan-Dec	1	n.a.	33.3	1) 31.22 2) 19.98 3) 20.81	1) 0.97 2) 0.62 3) 0.65	1) 7.49 2) 4.80 3) 5.00	n.a.	Seed unit: 100.000 seeds Seedling rate: 1 – 1.3 seed unit/ha TGW: 24-33 g/1000 seeds Slurry volume: 8-20L/100 kg seeds Max. 43.3 ml product/ha
		F		Sowing	BBCH 00 March-April								
		n.a.		Transplanting	n.a.								

Remarks table heading:

(a) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(b) Catalogue of pesticide formulation types and international coding system CropLife International Technical Monograph n°2, 6th Edition Revised May 2008
(c) g/kg or g/l
(d) Select relevant
(e) Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1
(f) No authorization possible for uses where the line is highlighted in grey, Use should be crossed out when the notifier no longer supports this use.

Remarks columns:

1 Numeration necessary to allow references

2 Use official codes/nomenclatures of EU Member States

3 For crops, the EU and Codex classifications (both) should be used; when relevant, the use situation should be described (e.g. fumigation of a structure)

4 F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

5 Scientific names and EPPO-Codes of target pests/diseases/ weeds or, when relevant, the common names of the pest groups (e.g. biting and sucking insects, soil born insects, foliar fungi, weeds) and the developmental stages of the pests and pest groups at the moment of application must be named.

6 Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated.

7 Growth stage at first and last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

8 The maximum number of application possible under practical conditions of use must be provided.

9 Minimum interval (in days) between applications of the same product

10 For specific uses other specifications might be possible, e.g.: g/m³ in case of fumigation of empty rooms. See also EPPO-Guideline PP 1/239 Dose expression for plant protection products.

11 The dimension (g, kg) must be clearly specified. (Maximum) dose of a.s. per treatment (usually g, kg or L product / ha).

12 If water volume range depends on application equipments (e.g. ULVA or LVA) it should be mentioned under “application: method/kind”.

13 PHI - minimum pre-harvest interval

14 Remarks may include: Extent of use/economic importance/restrictions

1.5.2. Details of other uses applied for to support the setting of MRLs for uses beyond the representative uses

No changes to GB MRLs for metalaxyl-M as a result of this amendment to approval.

Level 2

Metalaxyl-M

2. SUMMARY OF ACTIVE SUBSTANCE HAZARD AND OF PRODUCT RISK ASSESSMENT

2.1. IDENTITY

Metalaxyl-M is the common name of Methyl(R)-2-{[(2,6 dimethylphenyl)methoxyacetyl]amino}propionate. Metalaxyl-M is a mixture of the R-enantiomer CGA 329351 (min. 92-91%) and the S-enantiomer CGA 351920 of the racemic compound metalaxyl. For further information see the renewal assessment report (RAR), 2014.

2.2. PHYSICAL AND CHEMICAL PROPERTIES

2.2.1. Summary of physical and chemical properties of the active substance

The physico-chemical properties of the active substance can be summarised as follows, as provided in the RAR 2014.

Appearance	purified a.s. : clear, pale yellow, viscous liquid with weak odour a.s. as manufactured (TC) : clear, light brown, viscous liquid with weak odour
Freezing point	- 38.7°C (glass transition temperature)
Boiling point	not determinable due to thermal decomposition
Temperature of decomposition	approx. 270°C
Relative density (20°C)	1.125
Vapour pressure (25°C)	3.3 10^{-3} Pa
Henry's law constant (25°C)	3.5 10^{-5} Pa.m^3 /mol
UV/VIS absorption (λmax)	266 nm (512 l.mol^{-1} .cm $^{-1}$) and 274 nm (477 l.mol^{-1} .cm $^{-1)}$ no absorption between 290 and 750 nm
Solubility in water (25°C)	26 g/l
Solubility in organic solvents (TC) (25°C)	n-hexane : 59 g/l toluene : completely miscible dichloromethane : completely miscible methanol : completely miscible n-octanol : completely miscible acetone : completely miscible ethyl acetate : completely miscible
Partition coefficient (log Pow) (25°C)	1.71

Hydrolysis (20°C)	hydrolytical stability up to pH 7 pH 9 : DT50 = 216 d
Direct phototransformation (25°C)	not significant
Quantum yield	not determined (ε < 1 l.mol-1 .cm -1 at 290 nm)
Dissociation constant	no pKa in an accesible pH-range
Stability in air	estimated DT50 in the atmosphere = between 4 and 6 h
Flammability/auto-flammability (TC)	auto-ignition temperature : 410°C
Flash point (TC)	179°C (1013 mbar)
Explosive properties (TC)	not explosive
Oxidizing properties (TC)	No oxidizing properties
Surface tension (TC) (20°C)	σ = 57.6 - 57.8 mN/m (1 g/l) (as manufactured)

2.2.2. Summary of physical and chemical properties of the plant protection product

The summary for the formulated products is presented in the Part A of the dRR.

Please refer to these for details.

2.3. DATA ON APPLICATION AND EFFICACY

For the 2014 renewal of approval, the applicant submitted all the relevant information to support outdoor use as a seed treatment for the representative formulations. Therefore, no further assessment is necessary with respect to this application. Further information may be required for GB authorisation of plant protection products containing Metalaxyl-M.

2.4. FURTHER INFORMATION

For this Article 7 amendment application, this section is unchanged from the assessment in the existing RAR dated 2014.

2.5. METHODS OF ANALYSIS

For this Article 7 amendment application, this section is unchanged from the assessment in the existing RAR dated 2014. Methods were submitted to support the data generated in the area of ecotoxicology, for more information see the dRR.

2.6. EFFECTS ON HUMAN AND ANIMAL HEALTH

2.6.1. Summary of absorption, distribution and excretion in mammals

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.6.2. Summary of acute toxicity

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.6.3. Summary of short-term toxicity

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.6.4. Summary of genotoxicity

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.6.5. Summary of long-term toxicity and carcinogenicity

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.6.6. Summary of reproductive toxicity

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.6.7. Summary of neurotoxicity

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.6.8. Summary of further toxicological studies on the active substance

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.6.9. Summary of toxicological data on impurities and metabolites

To address the genotoxicity concern identified for impurity CGA226048 in the in vitro

chromosome aberration assay ([redacted], 2005) from the renewal of approval (see RAR 2014) an in vivo micronucleus study was submitted by the applicant. This study has been evaluated below by HSE. HSE has concluded that the test item did not induce micronuclei up to the limit dose of 2000 mg/kg bw as determined by the mammalian bone marrow micronucleus test in the mouse. Exposure of the bone marrow was demonstrated by the presence of the test item in blood. Therefore, CGA226048 is non-genotoxic in this bone marrow micronucleus assay.

Overall conclusion on the toxicological relevance assessment of impurity CGA226048 and its maximum content in the technical material.

The genotoxic potential of impurity CGA226048 was investigated during the renewal of approval assessment via in vitro in an Ames test, a mouse lymphoma assay and a chromomosme aberration study. The impurity was negative in the Ames test and mouse lymphoma assay, but was weakly/equivocally positive in the chromosome aberration study. However, in a modern in vivo micronucleus study submitted by the applicant for this amendment application, the clastogenicity of the impurity observed in vitro was not confirmed in vivo. Overall, impurity CGA226048 is not genotoxic and no longer toxicologically relevant. Therefore, the previously specified limit of 0.18 g/kg is no longer needed and the impurity can be specified in the technical material at a maximum level of 15 g/kg, in line with the 5-batch analysis and Quality Control data.

2.6.10. Summary of medical data and information

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.6.11. Toxicological end point for assessment of risk following long-term dietary exposure - ADI

The ADI was set at 0.08mg/kg bw per day during the renewal of approval assessment (EFSA Conclusion, 2015). There is no change to this endpoint based on the information submitted for this GB assessment.

2.6.12. Toxicological end point for assessment of risk following acute dietary exposure - ARfD (acute reference dose)

The ADI was set at 0.5mg/kg bw per day during the renewal of approval assessment (EFSA Conclusion, 2015). There is no change to this endpoint based on the information submitted for this GB assessment.

2.6.13. Toxicological end point for assessment of occupational, bystander and residents risks – AOEL

The ADI was set at 0.08mg/kg bw per day during the renewal of approval assessment (EFSA Conclusion, 2015). There is no change to this endpoint based on the information submitted for this GB assessment.

2.6.14. Toxicological end point for assessment of occupational, bystander and residents risk - AAOEL

No AAOEL was set during the renewal of approval assessment (EFSA Conclusion, 2015). There is no change to this endpoint based on the information submitted for this GB assessment.

2.6.15. Summary of product exposure and risk assessment

The summary of the assessments undertaken for the products 'Wakil XL' and 'Vibrance SB' are presented in the Part A of the dRR.

2.7. RESIDUE

The summary of the assessments undertaken for the products 'Wakil XL' and 'Vibrance SB' are presented in the Part A of the dRR.

2.8. FATE AND BEHAVIOUR IN THE ENVIRONMENT

The summary of the assessments undertaken for the products 'Wakil XL' and 'Vibrance SB' are presented in the Part A of the dRR.

It should be noted that the applicant requested a refinement to the formation fraction to metabolite SYN546520 from 0.47 to 0.1. Whilst the applicant submitted data in support of this refinement, the data were not evaluated. This is because there was no clear need for this refinement in the risk assessment for either of the representative products and GAPs evaluated in this submission ('Vibrance SB' used on sugar beet and 'Wakil XL' used on peas). If the applicant can demonstrate a need for this refinement in future submissions for metalaxyl-M containing products, then the data can be evaluated at that time.

2.9. EFFECTS ON NON-TARGET SPECIES

As a result of the EU renewal of approval of metalaxyl-M, a restriction was stipulated that seeds treated with metalaxyl-M shall only be sown in greenhouses. This

restriction was considered necessary due to risks to birds and mammals from consumption of treated seed.

Risks to birds and mammals from consumption of seedlings were considered acceptable for representative crops spinach and sunflowers, provided seedlings were planted out 21 days or more after sowing.

Concerns were also raised regarding risk from metabolites. EFSA considered that the risk assessment for representative products 'Ridomil Gold MZ WG' and 'Apron XL' did not transparently address the risk to birds and mammals from major plant metabolites (EFSA, 2015). However, taking into account the RMS assessment of metabolites, which showed metabolites all have low *log* Kow values indicating low potential for bioaccumulation, this point was considered addressed.

Therefore, due to the risks identified to birds and mammal, the implementing regulation for the renewal of metalaxyl-M specifies that when used for seed treatment, only the treatment of seeds intended to be sown in greenhouses may be authorised. In order to address risks to birds and mammals via consumption of seedlings, a minimum period before transplanting outdoors seedlings grown from treated seed (21 days for spinach).

Under this Article 7 application, the applicant is seeking to amend the conditions of approval: removing the restriction that only the treatment of seeds intended to be sown in greenhouses may be authorised. New data and risk assessments have been provided in order to demonstrate that outdoor sowing of seed treated with metalaxyl-M will not result in unacceptable impacts on birds and mammals.

2.9.1. Summary of effects on birds and other terrestrial vertebrates

Effects on Birds

Avian toxicity endpoints from the EU renewal of metalaxyl-M are reported in the following table.

Avian endpoints for metalaxyl-M

Species	Substance	Exposure system	Results	Reference
Bobwhite quail (*Colinus virginianus*)	Metalaxyl-M	Acute toxicity	LD_{50} = 1419 mg/kg bw	EFSA Journal 2015;13(3):3999 [redacted], 1995; CGA329351/0310
Bobwhite quail (*Colinus virginianus*)	Metalaxyl-M	Acute toxicity	LD_{50} = 981 mg/kg bw	EFSA Journal 2015;13(3):3999 [redacted] *et al*., 1995; CGA329351/0301
Geometric mean bobwhite quail		Acute toxicity	**LD_{50} = 1180 mg/kg bw**	EFSA Journal 2015;13(3):3999

Mallard duck (*Anas platyrhynchos*)	Metalaxyl	Acute toxicity	LD_{50} = 1466 mg/kg bw	EFSA Journal 2015;13(3):3999; [redacted], 1977; CGA48988/0149
Bobwhite quail (*Colinus virginianus*)	'Ridomil Gold'	Acute toxicity (extrapolated)	LD_{50} = 3228 mg/kg bw	EFSA Journal 2015;13(3):3999; [redacted] & [redacted], 2005; CGA329351/2154
Bobwhite quail (*Colinus virginianus*)	Metalaxyl-M	Dietary 8 d Short-term	LD_{50} > 5620 mg/kg food (> 2631 mg/kg bw/d)	EFSA Journal 2015;13(3):3999; [redacted] *et.al*, 1995a; CGA329351/0302
Japanese quail (*Coturnix japonica*)	Metalaxyl		LD_{50} > 10 000 mg/kg food	EFSA Journal 2015;13(3):3999; [redacted], 1976; CGA48988/0154
Bobwhite quail (*Colinus virginianus*)	Metalaxyl		LD_{50} > 10 000 mg/kg food	EFSA Journal 2015;13(3):3999; [redacted], 1977a; CGA48988/0147
Mallard duck (*Anas platyrhynchos*)	Metalaxyl		LD_{50} > 10 000 mg/kg food	EFSA Journal 2015;13(3):3999; [redacted], 1977b; CGA48988/1998
Bobwhite quail (*Colinus virginianus*)	Metalaxyl-M	Dietary Reproductive toxicity	NOEL = 900 mg/kg food (84 mg/kg bw/d)	EFSA Journal 2015;13(3):3999; [redacted] and [redacted], 1998; CGA329351/1071
Mallard duck (*Anas platyrhynchos*)	Metalaxyl-M		NOEL = 900 mg/kg food (117.3 mg/kg bw/d)	EFSA Journal 2015;13(3):3999; [redacted] and [redacted], 1998a; CGA329351/1072
Bobwhite quail (*Colinus virginianus*)	Metalaxyl		NOEL = 900 mg/kg food (no mg/kg bw/day figure presented in EFSA (2015))	EFSA Journal 2015;13(3):3999; [redacted], 1980a; CGA48988/0151
Mallard duck (*Anas platyrhynchos*)	Metalaxyl		NOEL = 300 mg/kg food (**24.6 mg/kg bw/d**)	EFSA Journal 2015;13(3):3999; [redacted], 1980b; CGA48988/0152

Acute toxicity:

According to EFSA (2015), the key acute endpoint is one based on the geometric mean of the available studies on bobwhite quail, i.e. an LD_{50} of 1180 mg a.s./kg bw. The applicant has proposed changing this and has referenced EFSA (2009), and in particular points 2.4.1 and 2.4.2, where the guidance document proposes that when multiple studies are available with different species an overall geometric mean can be determined.

In addition to studies with the bobwhite quail, a study was conducted with the mallard duck (*Anas platyrhynchos*) in which an LD_{50} of 1466 mg/kg bw/day was determined. Using these two endpoints (i.e. LD_{50} of 1180 mg/kg bw and LD_{50} of 1466 mg/kg bw), and in accordance with the EFSA guidance (2009), the applicant proposes that an overall geometric mean of 1315 mg/kg bw/day should be used in the acute risk assessment.

Due to shortcomings with the study, HSE has not revisited the mallard duck study and will retain the EU agreed acute toxicity endpoint, i.e. the bobwhite quail geometric mean LD_{50} = 1180 mg a.s./kg bw, for use in the risk assessment.

Long-term/ reproductive toxicity:

The EU renewal for metalaxyl-M identified a critical NOEC of 300 mg a.s./kg food, equivalent to a NOEL of 24.6 mg/kg bw/d, from a study with mallard duck ([redacted]**, 1980b**). The applicant has proposed revising the NOEL used in the avian long-term/reproductive risk assessment to 84 mg/kg bw/d, derived from a study with bobwhite quail ([redacted] **and** [redacted]**, 1998**). In order to consider this proposal, HSE has reviewed the underlying data and new historic control data provided.

When metalaxyl-M underwent renewal, four avian reproduction studies were considered: [redacted] (1980a), [redacted] (1980b), [redacted] and [redacted] (1998a) and [redacted] and [redacted] (1998b). The former two studies tested metalaxyl, while the latter tested metalaxyl-M. However, all studies were considered relevant during the EU peer review of metalaxyl-M and the mallard duck study ([redacted], 1980b) provided the lowest NOEL and was considered sufficiently reliable to set the critical endpoint for use in risk assessment.

Regarding the mallard duck study ([redacted], 1980b), the applicant has raised concerns regarding the age of birds, housing of multiple males per pen, shorter egg collection period, insufficient replication, environmental conditions, lack of analytical verification of the test item, and comparison of results with historic control data. HSE has reviewed these points but concludes that whilst the study is not up to the same standard as modern studies, it is not considered sufficiently unreliable to reject the study, especially as potentially adverse effects were observed.

Effects seen in the [redacted] (1980b) were considered alongside the other 3 studies available. Uncertainties are identified with all four studies but they each contain potentially relevant information for the risk assessment. Key effects observed across the studies were on chick body weight, adult body weight, eggshell thickness, and embryo/hatchling effects. When considering all four studies together, HSE concludes

that retaining the NOEL of 24.6 mg a.s./kg bw/d from the renewal review remains appropriate for metalaxyl-M.

Effects on terrestrial vertebrates other than birds

Mammalian toxicity endpoints from the EU renewal of metalaxyl-M are reported in the following table.

Mammalian endpoints for Metalaxyl-M

Species	Substance	Exposure system	Results	Reference
Rat	Metalaxyl-M	Oral 1 d Acute	LD_{50} = 953 mg/kg bw (male) **LD_{50} = 375 mg/kg bw** (female)	EFSA Journal 2015;13(3):3999; [redacted], 1994; CGA329351/0002
Rat	Metalaxyl-M	Dietary Reproductive toxicity	**NOAEL = 96 mg/kg bw/d**	EFSA Journal 2015;13(3):3999; [redacted] *et al*., 1980; CGA48988/0597

Acute toxicity:

Mammalian acute oral studies have been carried out with metalaxyl-M and with the EU representative formulation 'Apron XL'. These studies were reviewed by the RMS in the EU renewal of metalaxyl-M and were summarised in Volume 3 section B.6 of the RAR. The lowest LD_{50} of 375 mg a.s./kg bw for females from the [redacted] (1994a) study will be used in the acute risk assessment for mammals. This is in line with the EU renewal review of metalaxyl-M.

It is noted that an acute oral toxicity study is also available for mice ([redacted], 1996d). In principle a geometric mean LD_{50} could be derived from the rat and mouse data. However, this is complicated by the fact that a precise LD_{50} was not determined for mice (LD_{50} = 500-1000 mg a.s./kg bw). If it were conservatively assumed that the LD_{50} for mouse was 500 mg a.s./kg, then the geometric mean using the mouse and rat values would be 433 mg a.s./kg bw/d. Therefore, the difference between this geometric mean LD_{50} and the rat-only value is minor and hence the rat-only value will be retained in the risk assessment.

Long-term/reproductive toxicity:

Mammalian short-term dietary and long-term reproduction studies have been carried out with either metalaxyl or metalaxyl-M. These studies were reviewed by the RMS in the EU renewal review of metalaxyl-M and were summarised in Volume 3 section B.6 RAR. From these data it was concluded for the EU renewal review of metalaxyl-M that the ecotoxicological toxicity to mammals of the enantiomer metalaxyl-M is comparable to that of the racemate metalaxyl. The lowest NOAEL of 96 mg a.s./kg

bw/d from the [redacted] et al. (1980) study will be used in the reproductive risk assessment for mammals. This is in line with the EU renewal review of metalaxyl-M.

It is noted that no reproductive toxicity studies are available with the current representative formulated products, however, no such studies are considered necessary and the risk assessment can be based on the active substance toxicity.

2.9.2. Summary of effects on aquatic organisms

No assessment required under this assessment. Methods of analysis unchanged from previous assessment on metalaxyl-M.

2.9.3. Summary of effects on arthropods

No assessment required under this Article 7 assesment. Methods of analysis unchanged from previous assessment on metalaxyl-M.

2.9.4. Summary of effects on non-target soil meso- and macrofauna

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.9.5. Summary of effects on soil nitrogen transformation

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.9.6. Summary of effects on terrestrial non-target higher plants

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.9.7. Summary of effects on other terrestrial organisms (flora and fauna)

No assessment required under this Article 7 assessemnt. Methods of analysis unchanged from previous assessment on metalaxyl-M.

2.9.8. Summary of effects on biological methods for sewage treatment

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.9.9. Summary of product exposure and risk assessment

Summary of Risk Assessment - Birds

Acute Risk Assessment

Risks to birds have been assessed in accordance with EFSA guidance on bird and mammal risk assessment (EFSA, 2009). The key metalaxyl-M toxicity endpoint for the acute risk assessment is as follows:

- Geometric mean LD_{50} = 1180 mg a.s./kg bw

First Tier - 'Vibrance SB'

For pelleted seeds, such as sugar and fodder beet, it is assumed that birds do not intentionally consume seeds for food but may consume pelleted seed as/with grit (EFSA, 2009). Therefore exposure of birds ingesting seeds as/with grit has been considered.

Tier 1 acute risk to birds – consumption of treated seeds with/as grit

Crop	Active substance	Generic focal species	$DGritD_{acute}$ (mg a.s./kg bw)	LD_{50} (mg/kg bw)	TER_A
Sugar and fodder beet	Metalaxyl-M	Large bird	6.07	1180	194.46

The acute TER is above the trigger value of 10. An acceptable acute risk to birds from the consumption of treated seed with/as grit had therefore been demonstrated.

Birds may also be exposed to metalaxyl-M via consumption of emerged seedlings.

Tier 1 acute risk to birds – consumption of emerged seedlings

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	LD_{50} (mg/kg bw)	TER_A
Sugar and fodder beet	Metalaxyl-M	Small omnivorous bird	19.98	1180	59.06
	Metalaxyl-M	Large herbivorous bird	11.99	1180	98.43

The acute TERs for all generic focal species are above the trigger value of 10. Acceptable acute risks to birds from the consumption of emerged seedlings have therefore been demonstrated.

Birds could also be exposed to metalaxyl-M via drinking water. The puddle scenario is relevant for birds taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. Since the ratio of the application rate to the toxicity endpoint is less than the

trigger value of 50, an acceptable acute risk to birds can be concluded for the puddle scenario and no further consideration is required.

Acute risk to birds from drinking water – puddle scenario

Substance	Crop	Application Rate (g/ha)	Endpoint (mg/kg bw)	Ratio AR (g/ha)/endpoint (mg/kg bw)	Trigger value
Metalaxyl-M	Sugar and fodder beet	0.62	LD_{50} = 1180	0.00053	≤ 50

First Tier - 'Wakil XL'

Birds may be exposed to metalaxyl-M when consuming vining pea seeds treated with 'Wakil XL' as a food source. Therefore exposure of birds ingesting seeds as food has been considered.

Tier 1 acute risk to birds – consumption of treated seeds

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	LD_{50} (mg/kg bw)	TER_A
Vining pea	Metalaxyl-M	Large granivorous bird	33.92	1180	34.79

The acute TER is above the trigger value of 10. Acceptable acute risks to birds from the consumption of treated seed have therefore been demonstrated.

Birds may also be exposed to metalaxyl-M via consumption of emerged seedlings.

Tier 1 acute risk to birds – consumption of emerged seedlings

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	LD_{50} (mg/kg bw)	TER_A
Vining pea	Metalaxyl-M	Small omnivorous bird	33.92	1180	34.79
	Metalaxyl-M	Large herbivorous bird	20.35	1180	57.98

The acute TERs for all generic focal species are above the trigger value of 10. Acceptable acute risks to birds from the consumption of emerged seedlings have therefore been demonstrated.

Birds could also be exposed to metalaxyl-M via drinking water. The puddle scenario is relevant for birds taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. Since the ratio of the application rate to the toxicity endpoint is less than the trigger value of 50, an acceptable acute risk to birds can be concluded for the puddle scenario and no further consideration is required.

Acute risk to birds from drinking water – puddle scenario

Substance	Crop	Application Rate (g/ha)	Endpoint (mg/kg bw)	Ratio AR (g/ha)/endpoint (mg/kg bw)	Trigger value
Metalaxyl-M	Vining pea	76.32	LD_{50} = 1180	0.0065	≤ 50

Long-term/reproductive risk assessment

The key metalaxyl-M toxicity endpoint for the long-term/reproductive risk assessment is as follows:

- NOAEL = 24.6 mg a.s./kg bw/d

First tier – Vibrance SB

For pelleted seeds, such as sugar and fodder beet, it is assumed that birds do not intentionally consume seeds for food but may consume pelleted seed as/with grit (EFSA, 2009). Therefore exposure of birds ingesting seeds as/with grit has been considered.

Tier I long-term/reproductive risk to birds – consumption of treated seeds with/as grit

Crop	Active substance	Generic focal species	$DGritD_{repro}$ (mg a.s./kg bw/d)	NOEL (mg/kg bw/d)	TER_{LT}
Sugar and fodder beet	Metalaxyl-M	Large granivorous bird	3.23	24.6	7.61

The Tier 1 long-term/reproductive TER_{LT} for large birds consuming treated seeds with/as grit is above the trigger of 5. No further consideration of the long-term reproductive risk to birds via consumption of seed with/as grit is required.

Birds may also be exposed to metalaxyl-M via consumption of emerged seedlings.

Tier 1 long-term/reproductive risk to birds – consumption of emerged seedlings

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	NOEL (mg/kg bw/d)	TER_{LT}
Sugar and fodder beet	Metalaxyl-M	Small omnivorous bird	19.98	24.6	**1.23**
	Metalaxyl-M	Large herbivorous bird	11.99	24.6	**2.05**

The Tier 1 long-term/reproductive TER_{LT} for birds consuming treated sugar and fodder beet seedlings are below the trigger of 5 for both generic focal species, indicating unacceptable risks. **Further consideration of the long-term/reproductive risk to birds from consumption of treated seedlings is therefore required**.

Birds could also be exposed to metalaxyl-M via drinking water. The puddle scenario is relevant for birds taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. Since the ratio of the application rate to the toxicity endpoint is less than the trigger value of 50, an acceptable long-term/reproductive risk to birds can be concluded for the puddle scenario and no further consideration is required.

Long-term/reproductive risk to birds from drinking water – puddle scenario

Substance	Crop	Application Rate (g/ha)	Endpoint (mg/kg bw/d)	Ratio AR (g/ha)/endpoint (mg/kg bw/d)	Trigger value
Metalaxyl-M	Sugar and fodder beet	0.62	NOEL = 24.6	0.025	≤ 50

Higher tier – Vibrance SB

The following areas of the assessment were not demonstrated to result in acceptable long-term/reproductive risks to birds and thus require further consideration:

- Long-term/reproductive risk to birds from exposure to metalaxyl-M via consumption of emerged seedlings.

The first tier assessment of the risk to birds via consumption of seedlings assumes that residues in the seeding are a factor of 5 times lower than residues in the seed (i.e. NAR/5). This is to account for dilution of residues in the growing seedling. To refine this risk, the applicant used a study by [redacted] **(2015)** to determine a crop-specific dilution factor to estimate seedling concentrations from seed loading. The use of a revised factor of 35.6 is accepted by HSE and TER values are updated accordingly.

Refined long-term/reproductive risk to birds – consumption of emerged seedlings

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	NOEL (mg/kg bw/d)	TER_{LT}
Sugar and fodder beet	Metalaxyl-M	Small omnivorous bird	2.81	24.6	8.75
	Metalaxyl-M	Large herbivorous bird	1.68	24.6	14.64

The resulting TER values are all above the trigger value of 5. Acceptable long-term/reproductive risks to birds from consumption of metalaxyl-M via crop seedlings are therefore indicated.

First tier – Wakil XL

Birds may be exposed to metalaxyl-M when consuming vining pea seeds treated with 'Wakil XL' as a food source. Therefore exposure of birds ingesting seeds as food has been considered.

Tier I long-term/reproductive risk to birds – consumption of treated seeds

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	NOEL (mg/kg bw/d)	TER_{LT}
Vining peas	Metalaxyl-M	Large granivorous bird	33.92	24.6	**0.73**

The Tier 1 long-term/reproductive TER_{LT} for large granivorous birds consuming treated vining pea seeds is below the trigger of 5 for metalaxyl-M. **Further consideration of the long-term/reproductive risk to birds from consumption of treated seed is therefore required.**

Birds may also be exposed to metalaxyl-M via consumption of emerged seedlings.

Tier 1 long-term/reproductive risk to birds – consumption of emerged seedlings

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	NOEL (mg/kg bw/d)	TER_{LT}
Vining peas	Metalaxyl-M	Small omnivorous bird	33.92	24.6	**0.73**
	Metalaxyl-M	Large herbivorous bird	20.35	24.6	**1.21**

The Tier 1 long-term/reproductive TER_{LT} for birds consuming treated vining pea seedlings are below the trigger of 5 for both generic focal species. **Further consideration of the long-term/reproductive risk to birds from consumption of treated seedlings is therefore required.**

Birds could also be exposed to metalaxyl-M via drinking water. The puddle scenario is relevant for birds taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. Since the ratio of the application rate to the toxicity endpoint is less than the trigger value of 50, an acceptable long-term/reproductive risk to birds can be concluded for the puddle scenario and no further consideration is required.

Long-term/reproductive risk to birds from drinking water – puddle scenario

Substance	Crop	Application Rate (g/ha)	Endpoint (mg/kg bw/d)	Ratio AR (g/ha)/endpoint (mg/kg bw/d)	Trigger value
Metalaxyl-M	Vining pea	76.32	NOEL = 24.6	3.1	≤ 50

Higher tier – Wakil XL

The following areas of the assessment were not demonstrated to result in acceptable long-term/reproductive risks to birds and thus require further consideration:

- Long-term/reproductive risk to birds from exposure to metalaxyl-M via consumption of seeds as food;
- Long-term/reproductive risk to birds from exposure to metalaxyl-M via consumption of emerged seedlings;

Long-term/reproductive risk to birds from exposure to metalaxyl-M via consumption of seeds as food

The Applicant proposed the following refinements to the risk assessment for granivorous birds:

1. Higher tier chronic avian toxicity endpoint for metalaxyl-M
2. Seed residue dissipation data

3. Selection of relevant focal species based on field study in freshly drilled pea fields
4. Fraction of diet obtained from the treated area (PT)

The avian long-term/reproductive toxicity endpoint is discussed above and it is concluded to be appropriate to retain the agreed endpoint from the EU renewal assessment of NOEL = 24.6 mg/kg bw/d.

Studies investigating the decline of metalaxyl-M on treated seeds are available for maize ([redacted], 2012) and spinach ([redacted] 2021a&b). Acknowledging the uncertainties regarding the available studies and extrapolation of data to vining peas, the residue decline information can still be used to inform the risk assessment. While a precise DT_{50} for vining peas cannot be determined, the data support use of a DT_{50} of 10 days in the higher tier risk assessment. This results in a time-weighted average factor of 0.53.

Based on results from a monitoring study conducted on pea fields in Northern France ([redacted] et al. 2006), the woodpigeon is considered an appropriate focal species. A PT value of 0.17 is determined to be appropriate for this focal species. This PT value is the worst-case value from the consumer bird population from a study investigating woodpigeon foraging behaviour in maize fields in north-west Germany ([redacted] & [redacted], 2018).

Taking into account these refinements, a revised TER_{LT} has been calculated for the woodpigeon focal species.

Refined risk assessment for woodpigeon from consumption of seed treated with metalaxyl-M

Crop	Focal species	FIR/bw	NAR	TWA	PT	DDD (mg/kg bw/d)	NOEL (mg/kg bw/d)	TER_{LT}
Vining pea	Woodpigeon	0.074	339.2	0.53	0.17	2.26	24.6	10.9

The resulting TER value is above the first tier trigger value of 5 by approximately a factor of 2. The refined exposure assessment is considered by HSE to be representative of the risk experienced by a realistic worst-case individual in an exposed population. In light of consideration of the uncertainties associated with the risk assessment and the magnitude of this TER, it is considered that the refined exposure assessment demonstrates that reproductive effects following exposure to metalaxyl-M are unlikely for this exposure route.

Long-term/reproductive risk to birds from exposure to metalaxyl-M via consumption of emerged seedlings

The applicant has proposed the following refinements to the risk assessment for herbivorous birds:

1. Higher tier chronic avian toxicity endpoint for metalaxyl-M
2. Seedling residue data
3. Selection of relevant focal species based on field study in freshly drilled pea fields
4. Fraction of diet obtained from the treated area (PT)

The avian long-term/reproductive toxicity endpoint is discussed above and it is concluded to be appropriate to retain the agreed endpoint from the EU renewal assessment of NOEL = 24.6 mg/kg bw/d.

The first tier assessment of the risk to birds via consumption of seedlings assumes that residues in the seeding are a factor of 5 times lower than residues in the seed (i.e. NAR/5). This is to account for dilution of residues in the growing seedling. To refine this risk, the applicant used a study by [redacted] (1999) to determine residues in pea seedlings following treatment of pea seeds with metalaxyl-M. The use of a residue in pea seedlings of 1.089-7.12 mg/kg is accepted by HSE for the higher tier risk assessment.

Based on results from a monitoring study conducted on pea fields in Northern France ([redacted] et al. 2006), the woodpigeon and skylark are considered to be appropriate focal species. For wood pigeon a PT value of 0.32 is determined to be appropriate for this focal species, based on radio-tracking data from maize fields ([redacted] & [redacted], 2018). For skylark a PT value of 0.879 is determined to be appropriate for this focal species, based on radio-tracking data from maize fields ([redacted], 2010).

Taking into account these refinements, revised TER_{LT} values have been calculated for the focal species.

Refined risk assessment for birds from consumption of crop seedlings containing metalaxyl-M

Focal species	FIR/bw	PD	Residue (mg/kg)	TWA	PT	DDD (mg/kg bw/d)	NOEL (mg/kg bw/d)	TER_{LT}
Skylark (mixed diet)	0.48	0.25	7.12	0.53	0.879	0.398	24.6	61.8
	0.48	0.25	1.09	0.53	0.879	0.061	24.6	404
Skylark (100% seedlings)	0.55	0.5	7.12	0.53	0.879	0.912	24.6	27
	0.55	0.5	1.09	0.53	0.879	0.14	24.6	176
Woodpigeon	0.79	1	7.12	0.53	0.32	0.954	24.6	25.8

Focal species	FIR/bw	PD	Residue (mg/kg)	TWA	PT	DDD (mg/kg bw/d)	NOEL (mg/kg bw/d)	TER_{LT}
	0.79	1	1.09	0.53	0.32	0.146	24.6	168

The resulting TER values are above the first tier trigger value of 5 by at least a factor of 5. The refined exposure assessment is considered by HSE to be representative of the risk experienced by a realistic worst-case individual in an exposed population. In light of consideration of the uncertainties associated with the risk assessment and the magnitude of the TERs, it is considered that the refined exposure assessment demonstrates that reproductive effects from exposure to metalaxyl-M are unlikely for this exposure route.

Summary of Risk Assessment - Mammals

Acute Risk Assessment

Risks to mammals have been assessed in accordance with EFSA guidance on bird and mammal risk assessment (EFSA, 2009). The key metalaxyl-M toxicity endpoint for the acute risk assessment is as follows:

- LD_{50} = 375 mg a.s./kg bw

First Tier - 'Vibrance SB'

For pelleted seeds (which includes sugar and fodder beet), consideration of the risk to mammals from consumption of treated seeds is not required. Mammals may however be exposed to metalaxyl-M via consumption of emerged seedlings.

Tier 1 acute risk to mammals – consumption of emerged seedlings

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	LD_{50} (mg/kg bw)	TER_A
Sugar and fodder beet	Metalaxyl-M	Small omnivorous mammal	9.59	375	39.1
	Metalaxyl-M	Large herbivorous mammal	15.98	375	23.46

The acute TERs for all generic focal species are above the trigger value of 10. Acceptable acute risks to mammals from the consumption of emerged seedlings have therefore been demonstrated.

Mammals could also be exposed to metalaxyl-M via drinking water. The puddle scenario is relevant for mammals taking water from puddles formed on the soil

surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. Since the ratio of the application rate to the toxicity endpoint is less than the trigger value of 50, an acceptable acute risk to mammals can be concluded for the puddle scenario and no further consideration is required.

Acute risk to mammals from drinking water – puddle scenario

Substance	Crop	Application Rate (g/ha)	Endpoint (mg/kg bw)	Ratio AR (g/ha)/endpoint (mg/kg bw)	Trigger value
Metalaxyl-M	Sugar and fodder beet	0.62	LD_{50} = 375	0.0017	≤ 50

First Tier - 'Wakil XL'

Mammals may be exposed to metalaxyl-M when consuming vining pea seeds treated with 'Wakil XL' as a food source. Therefore exposure of mammals ingesting seeds as food has been considered.

Tier 1 acute risk to mammals – consumption of treated seeds

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	LD_{50} (mg/kg bw)	TER_A
Vining pea	Metalaxyl-M	Small omnivorous mammal	81.41	375	**4.61**

The acute TER for metalaxyl-M is below the trigger value of 10. **Further consideration is required for the acute risk to mammals from the consumption of treated seed.**

Mammals may also be exposed to metalaxyl-M via consumption of emerged seedlings.

Tier 1 acute risk to mammals – consumption of emerged seedlings

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	LD_{50} (mg/kg bw)	TER_A
Vining pea	Metalaxyl-M	Small omnivorous mammal	16.28	375	23.03
	Metalaxyl-M	Large herbivorous mammal	27.14	375	13.82

The acute TERs for all generic focal species are above the trigger value of 10. Acceptable acute risks to mammals from the consumption of emerged seedlings have therefore been demonstrated.

Mammals could also be exposed to metalaxyl-M via drinking water. The puddle scenario is relevant for mammals taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. Since the ratio of the application rate to the toxicity endpoint is less than the trigger value of 50, an acceptable acute risk to mammals can be concluded for the puddle scenario and no further consideration is required.

Acute risk to mammals from drinking water – puddle scenario

Substance	Crop	Application Rate (g/ha)	Endpoint (mg/kg bw)	Ratio AR (g/ha)/endpoint (mg/kg bw)	Trigger value
Metalaxyl-M	Vining pea	76.32	LD_{50} = 375	0.20	≤ 50

Higher tier – Wakil XL

The following areas of the assessment were not demonstrated to result in acceptable acute risks to mammals and thus require further consideration:

- Acute risk to mammals from exposure to metalaxyl-M via consumption of seeds as food.

The Applicant has proposed for the following refinements to the risk assessment for granivorous mammals:

1. Focal species – wood mouse
2. PD (proportion of food type in the diet) refinement wood mouse
3. Additional weight of evidence:
    a. Dehusking behaviour of wood mouse
    b. Lower formulation toxicity compared to predicted toxicity

Based on the available field monitoring studies, HSE accepts the selection of wood mouse as an appropriate focal species for small omnivorous mammals with the potential to consume vining pea seeds.

Refinement of the PD parameter is not accepted since including a mixed diet composition, that is averaged across a longer time period, has the potential to underestimate the acute risk to mammals.

Residues on treated seeds will be mainly located on the outside of the seeds (husk, testa, pericarp), whereas concentrations in the inner parts of the seeds (endosperm,

embryo) will be significantly lower. Thus, exposure of granivorous mammals may be markedly reduced if they dehusk seeds before consumption. The available data on dehusking behaviour by wood mice has been reviewed. There is some evidence to indicate that dehusking behaviour can reduce exposure of wood mice to a seed treatment applied to pea seeds under controlled conditions. However, there are a number of factors that result in a high degree of uncertainty when extrapolating these dehusking results to the metalaxyl-M risk assessment.

The applicant has referred to a study of the acute toxicity of the formulation 'Wakil XL' to rats. However, the formulation contains other active substances and for this Article 7 evaluation only the risk from the metalaxyl-M component of the formulation is under consideration. When the formulation toxicity endpoint is expressed just in terms of exposure to metalaxyl-M, the resulting LD_{50} is similar to the LD_{50} from the metalaxyl-M study.

Taking into account the agreed refinement, a revised TER value has been calculated.

Acute risk to wood mice exposed to residues of metalaxyl-M via the consumption of treated seeds of vining peas

Focal species	FIR/bw	Nominal application rate (mg/kg bw/d)	DDD (mg/kg bw/d)	LD_{50} (mg/kg bw)	TER_A
Wood mouse	0.21	339.2	71.23	375	**5.26**

The resulting higher tier TER remains below the first tier trigger value of 10, indicating that it has not been demonstrated that there is no unacceptable risk. If the geometric mean LD_{50} from the rat and mouse data was used in the above calculation (LD_{50} = 433 mg a.s./kg), the resulting TER would be 6.08, i.e. still below the trigger value. This refined exposure assessment is considered by HSE to be representative of the risk experienced by a realistic worst-case individual in an exposed population.

It has been calculated that a wood mouse would need to consume 10.7 treated seeds to exceed the acute regulatory dose (i.e. LD_{50}/10). This is considered a relatively small number of seeds that could conceivably be consumed by a wood mouse in a single feeding bout. No information is available on vining pea seed availability on the soil surface following drilling. Therefore, it is not possible to determine the area that would need to be foraged by a wood mouse to encounter 10.7 seeds on the soil surface.

Taking into account the refined TER value, dehusking data, and in light of consideration of the uncertainties associated with the risk assessment, it is concluded that it has not been demonstrated that any mortality is unlikely following exposure of small mammals to vining pea seeds treated with 'Wakil XL'. **HSE therefore concludes that it has not been clearly established that use of**

metalaxyl-M as a vining pea seed treatment will have no unacceptable impact on small mammals exposed to treated seed.

Long-term/reproductive risk assessment

Risks to mammals have been assessed in accordance with EFSA guidance on bird and mammal risk assessment (EFSA, 2009). The key metalaxyl-M toxicity endpoint for the long-term/reproductive risk assessment is as follows:

- NOAEL = 96 mg a.s./kg bw/d

First Tier - 'Vibrance SB'

For pelleted seeds (which includes sugar and fodder beet), consideration of the risk to mammals from consumption of treated seeds is not required. Mammals may however be exposed to metalaxyl-M via consumption of emerged seedlings.

Tier 1 long-term/reproductive risk to mammals – consumption of emerged seedlings

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	NOAEL (mg/kg bw/d)	TER_{LT}
Sugar and fodder beet	Metalaxyl-M	Small omnivorous mammal	9.59	96	10.01
	Metalaxyl-M	Large herbivorous mammal	15.98	96	6.01

The Tier 1 long-term/reproductive TER_{LT} for mammals consuming treated sugar and fodder beet seedlings are above the trigger of 5 for all generic focal species. Acceptable long-term/reproductive risks to mammals consuming treated seeds can be concluded.

Mammals could also be exposed to metalaxyl-M via drinking water. The puddle scenario is relevant for mammals taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. Since the ratio of the application rate to the toxicity endpoint is less than the trigger value of 50, an acceptable long-term/reproductive risk to mammals can be concluded for the puddle scenario and no further consideration is required.

Long-term/reproductive risk to mammals from drinking water – puddle scenario

Substance	Crop	Application Rate (g/ha)	Endpoint (mg/kg bw/d)	Ratio AR (g/ha)/endpoint (mg/kg bw/d)	Trigger value
Metalaxyl-M	Sugar and fodder beet	0.62	NOAEL = 96	0.0065	≤ 50

First Tier - 'Wakil XL'

Mammals may be exposed to metalaxyl-M when consuming vining pea seeds treated with 'Wakil XL' as a food source. Therefore exposure of mammals ingesting seeds as food has been considered.

Tier 1 long-term/reproductive risk to mammals – consumption of treated seeds

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	NOAEL (mg/kg bw/d)	TER_{LT}
Vining pea	Metalaxyl-M	Small omnivorous mammal	81.41	96	**1.18**

The Tier 1 long-term/reproductive TER_{LT} for small omnivorous mammals consuming treated vining pea seeds is below the trigger of 5 for metalaxyl-M. **Further consideration of the long-term/reproductive risk to mammals from consumption of treated seed is therefore required.**

Mammals may also be exposed to metalaxyl-M via consumption of emerged seedlings.

Tier 1 long-term/reproductive risk to mammals – consumption of emerged seedlings

Crop	Active substance	Generic focal species	DDD (mg/kg bw/d)	NOAEL (mg/kg bw/d)	TER_{LT}
Vining pea	Metalaxyl-M	Small omnivorous mammal	16.28	96	5.90
	Metalaxyl-M	Large herbivorous mammal	27.14	96	**3.54**

The Tier 1 long-term/reproductive TER_{LT} for mammals consuming treated vining pea seedlings are above the trigger of 5 for the small omnivore but below the trigger value for the large herbivore. **Further consideration of the long-term/reproductive risk to large herbivores via consumption of pea seedlings is therefore required.**

Mammals could also be exposed to metalaxyl-M via drinking water. The puddle scenario is relevant for mammals taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. Since the ratio of the application rate to the toxicity endpoint is less than the trigger value of 50, an acceptable long-term/reproductive risk to mammals can be concluded for the puddle scenario and no further consideration is required.

Long-term/reproductive risk to mammals from drinking water – puddle scenario

Substance	Crop	Application Rate (g/ha)	Endpoint (mg/kg bw/d)	Ratio AR (g/ha)/endpoint (mg/kg bw/d)	Trigger value
Metalaxyl-M	Vining pea	76.32	NOAEL = 96	0.8	≤ 50

Higher tier – Wakil XL

The following areas of the assessment were not demonstrated to result in acceptable long-term/reproductive risks to mammals and thus require further consideration:

- Long-term/reproductive risk to mammals from exposure to metalaxyl-M via consumption of seeds as food;
- Long-term/reproductive risk to mammals from exposure to metalaxyl-M via consumption of emerged seedlings.

Long-term/reproductive risk to mammals from exposure to metalaxyl-M via consumption of seeds as food

The Applicant has proposed the following refinements to the risk assessment for granivorous mammals:

1. Focal species – wood mouse
2. Seed residue dissipation data
3. PD refinement based on published literature data
4. PT refinement based on field studies

Based on the available field monitoring studies, HSE accepts the selection of wood mouse as an appropriate focal species for small omnivorous mammals with the potential to consume vining pea seeds.

The available data on dissipation of residues from seeds treated with metalaxyl-M are discussed above in the bird risk assessment section. It is concluded that a DT_{50} of 10 days and associated 21-day TWA of 0.53 can be used in the higher tier risk assessment.

The first tier risk assessment assumes that PT equals 1.0, i.e. the mammal obtains all its food from the treated crop. However, it is likely that the focal species will not feed exclusively in vining pea fields – part of its diet being obtained in other crops/habitats (i.e. PT < 1.0). Radio-tracking studies investigating wood mouse foraging behaviour in pre-emergence crop fields are available and have been reviewed. While there are uncertainties with the use of these datasets for the current risk assessment, use of a refined PT value of 0.51 is accepted for the higher tier risk assessment.

Studies investigating wood mouse diets have been reviewed ([redacted] **1979;** [redacted]**, 1989;** [redacted] **&** [redacted]**, 1998**). However, none of these studies include data on food items taken from post-drilling, pre-emergence fields specifically. There is also the potential to double-count the impact of PD, if refining both the PT and PD parameters in the risk assessment. Therefore, for these reasons, refinement of the PD parameter has not been accepted by HSE.

Taking into account the agreed refinements, a revised TER value has been calculated.

Long-term/reproductive risk to wood mice exposed to residues of metalaxyl-M via the consumption of treated seeds of vining peas

Focal species	FIR/bw	Nominal application rate (mg/kg bw/d)	PT	TWA	DDD (mg/kg bw/d)	NOAEL (mg/kg bw/d)	TER_{LT}
Wood mouse	0.21	339.2	0.51	0.53	19.25	96	**4.99**

The resulting higher tier TER value for the vining pea use is almost exactly equal to the standard first tier trigger value of 5. The refined exposure assessment is considered by HSE to be representative of the risk experienced by a realistic worst-case individual in an exposed population. Given the refined TER value is essentially equal to the trigger value and in light of a consideration of uncertainties indicating that there are more factors that would lead to the 'true' risk being overestimated rather than underestimated, it is concluded that the refined exposure assessment demonstrates that any reproductive effects are unlikely via this exposure route.

Long-term/reproductive risk to mammals from exposure to metalaxyl-M via consumption of emerged crop seedlings

The Applicant has proposed refining the growth dilution factor used in estimating the metalaxyl-M residue in emerged vining pea seedlings. To support this refinement data from Volllmin (1999) have been used and are considered in the higher tier risk assessment section for birds. Revised TER values have been calculated, taking into account residue values from Volllmin (1999).

Higher tier long-term/reproductive risk to mammals – consumption of emerged seedlings

Generic focal species	FIR/bw	Residue (mg/kg)	DDD (mg/kg bw/d)	NOAEL (mg/kg bw/d)	TER_{LT}
Large herbivorous mammal	0.4	1.089	0.436	96	220
	0.4	7.12	2.85	96	33.7

The resulting TER values are above the trigger value of 5, regardless of which of the residue values is used. Given the margin of safety in the refined risk assessment and the fact that only a single parameter has been refined compared to the first tier assessment, it is considered that the higher tier risk assessment is sufficient basis to conclude that any reproductive effects are unlikely from exposure via consumption of vining pea seedlings.

Overall conclusions of the risk assessment for birds and mammals

The overall outcomes of the risk assessments for birds and other terrestrial vertebrates are summarised in the following tables. For the proposed use of 'Vibrance SB' as a sugar beet seed treatment it has been demonstrated that there will be no unacceptable impacts on terrestrial vertebrates for all exposure scenarios. For the proposed use of 'Wakil XL' as a vining pea seed treatment, while for most scenarios it is concluded that there will be no unacceptable impacts on terrestrial vertebrates, it has not been demonstrated that there will be no unacceptable impact to mammals from acute exposure via consumption of treated seed.

It is noted that in light of risk assessment for the consumption of seedlings scenario conducted in this amendment evaluation, no time interval is necessary before seedlings grown under full and permanent protection can be planted outside.

Summary of risk assessment conclusions for use of Vibrance SB on sugar beet and fodder beet

Exposure route	Birds		Mammals	
	Acute	Long-term/ reproductive	Acute	Long-term/ reproductive
Ingestion of treated seed	No unacceptable impact demonstrated at first tier	No unacceptable impact demonstrated at first tier	No assessment required	No assessment required
Ingestion of germinated seedlings	No unacceptable impact demonstrated at first tier	No unacceptable impact concluded at higher tier	No unacceptable impact demonstrated at first tier	No unacceptable impact demonstrated at first tier

Exposure route	Birds		Mammals	
	Acute	Long-term/ reproductive	Acute	Long-term/ reproductive
Ingestion of drinking water	No unacceptable impact demonstrated at screening step	No unacceptable impact demonstrated at screening step	No unacceptable impact demonstrated at screening step	No unacceptable impact demonstrated at screening step

Summary of risk assessment conclusions for use of Wakil XL on vining pea

Exposure route	Birds		Mammals	
	Acute	Long-term/ reproductive	Acute	Long-term/ reproductive
Ingestion of treated seed	No unacceptable impact demonstrated at first tier	No unacceptable impact concluded at higher tier	Unacceptable impact cannot be excluded	No unacceptable impact concluded at higher tier
Ingestion of germinated seedlings	No unacceptable impact demonstrated at first tier	No unacceptable impact concluded at higher tier	No unacceptable impact demonstrated at first tier	No unacceptable impact concluded at higher tier
Ingestion of drinking water	No unacceptable impact demonstrated at screening step	No unacceptable impact demonstrated at screening step	No unacceptable impact demonstrated at screening step	No unacceptable impact demonstrated at screening step

2.10. CLASSIFICATION AND LABELLING

For this Article 7 amendment application, the classification and labelling is unchanged from the assessment in the RAR dated 2014.

2.11. RELEVANCE OF METABOLITES IN GROUNDWATER

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.12. CONSIDERATION OF ISOMERIC COMPOSITION IN THE RISK ASSESSMENT

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

2.13. RESIDUE DEFINITIONS

For this Article 7 amendment application, this section is unchanged from the assessment in the RAR dated 2014.

Level 3

Metalaxyl-M

3. PROPOSED DECISION

3.1. BACKGROUND TO THE PROPOSED DECISION

3.1.1. Proposal on acceptability against the decision making criteria – Article 4 and annex II of retained regulation (EC) No 1107/2009

It is considered that Article 4 of Assimilated Regulation (EC) No 1107/2009 is complied with. Specifically, the competent authority considers that the criteria continue to be met for the amended approval. In reaching this decision, the competent authority relies upon new information considered under this assessment as well as the extant from the last renewal of approval.

For use as seed treatment, no unacceptable risks to birds and mammals from exposure via the consumption of treated seeds are expected considering the represented formulation 'Vibrance SB' considered for this application.

For professional use as a fungicide for the representative formulation 'Wakil XL' on vining pea, it cannot be concluded that there will be no unacceptable effects on the environment, as provided for in Article 4(3)(e) of retained Regulation (EC) No 1107/2009, based on the HSE assessment.

It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with and it is considered that authorisation is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses, without condition or restriction.

3.1.2. Proposal – Candidate for substitution

Metaxaly-M does not meet the criteria for a candidate for substitution, as concluded for the renewal of approval. No information provided for this amendment application alters the previous conclusions.

3.1.3. Proposal – Low risk active substance

Active substance does not meet low risk criteria, see RAR 2014 for further details.

3.1.4. List of studies to be generated, still ongoing or available but not peer reviewed

N/A for this application.

3.1.5. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) No 546/2011, and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

There are no issues that could not be finalised following the assessment of this application for amendment of approval.

3.1.6. Critical areas of concern

The critical areas of concern identified are outlined in the table below:

Critical area of concern identified		Relevance in relation to representative use(s)
1	Acute risk to mammals via ingestion of treated seeds cannot be excluded.	Seed treatment in vining pea

3.1.7. Area(s) where expert consultation is considered necessary

This assessment has not required expert consultation.

3.2. PROPOSED DECISION

It is proposed that:

Under the assimilated Regulation (EC) No 1107/2009, the approval of Metalaxyl-M in GB can be amended to remove the following restriction:

When used for seed treatment, only the treatment of seeds intended to be sown in greenhouses may be authorised.

It is considered that the following impurity identified in technical metaxaly-M is **not** considered to be of toxicological or ecotoxicological relevance:

2-[(2,6-dimethyl-phenyl)-(2- methoxyacetyl)-amino]-propionic acid 1-methoxycarbonyl- ethyl ester (impurity CGA 226048). Therefore, the approval can be amended to remove the inclusion of this impurity.

NOA409045 has also been removed as a relevant groundwater metabolite.

It is proposed that the following be specified as areas requiring particular attention when evaluating applications for product authorisation(s):

- The risk to birds and other terrestrial vertebrates from products applied as seed treatments. In particular, acute risk to mammals via ingestion of treated seeds. An acceptable risk in this area was not demonstrated for the representative formulation 'Wakil XL'. Therefore, particular attention will be required in this area when assessing applications for product authorisations.

The list of data gaps identified during the peer review process for the renewal of metalaxyl-M, presented in the EFSA Conclusion (2015) are still applicable to GB where relevant.

3.3. RATIONAL FOR THE CONDITIONS AND RESTRICTIONS TO BE ASSOCIATED WITH THE APPROVAL OR AUTHORISATION(S), AS APPROPRIATE

3.3.1. Particular conditions proposed to be taken into account to manage the risks identified within this Article 7 amendment application

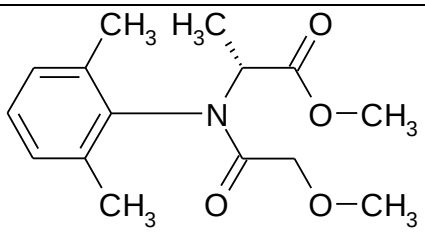
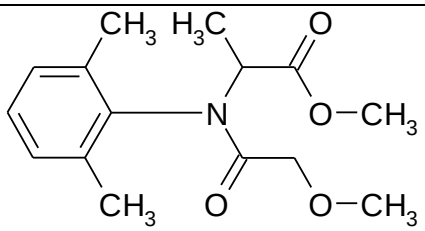
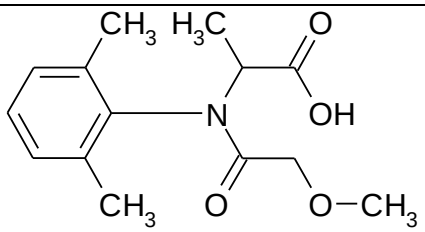
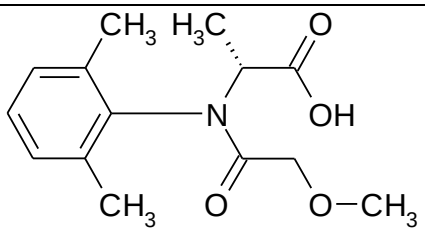
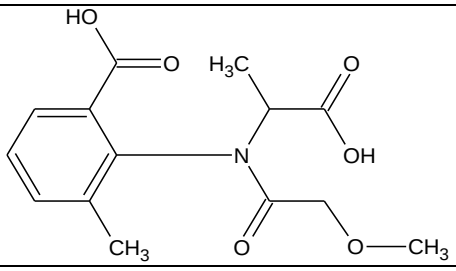
Proposed condition/risk mitigation measure	Relevance in relation to representative use(s)
To protect birds and wild mammals, treated seed should not be left on the soil surface. Bury or remove spillages. Treated seed should not be broadcast	Vibrance SB on sugar and fodder beet.

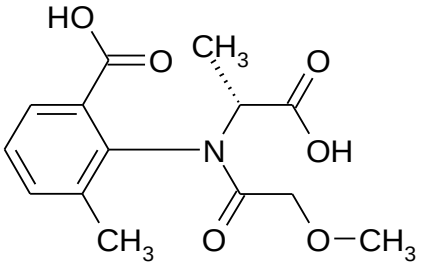
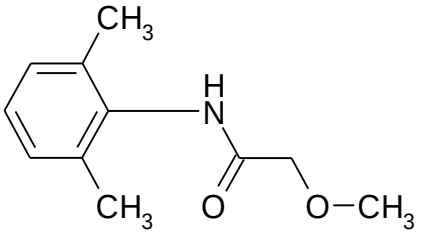
3.4. APPENDICES

GUIDANCE DOCUMENTS USED IN THIS ASSESSMENT

All relevant extant guidance documents in place on 22nd October 2021 were relied upon in this assessment.

3.4.1. Metabolites and their codes

Chemical Name	Code	Structural Formula
(R)-2-[(2,6-Dimethyl-phenyl)-(2-methoxy-acetyl)-amino]-propionic acid methyl ester	CGA329351	
(RS)-2-[(2,6-Dimethyl-phenyl)-(2-methoxy-acetyl)-amino]-propionic acid methyl ester	CGA48988	
(RS)-2-[(2,6-Dimethyl-phenyl)-(2-methoxy-acetyl)-amino]-propionic acid	CGA62826	
(R)-2-[(2,6-Dimethyl-phenyl)-(2-methoxy-acetyl)-amino]-propionic acid	NOA409045	
2-[((RS)-1-Carboxy-ethyl)-(2-methoxy-acetyl)-amino]-3-methyl-benzoic acid	CGA108906	

2-[((R)-1-Carboxy-ethyl)-(2-methoxy-acetyl)-amino]-3-methyl-benzoic acid	SYN546520	
N-[(2,6-Dimethyl-phenyl)-2-methoxy-acetamide	CGA67868	

3.5. REFERENCE LIST